

### **REMARKS**

As an initial matter, Applicants request withdrawal of the finality of the outstanding final office action. Respectfully, the finality of the instant Office Action is not proper in view of MPEP 706.07(a) as cited by the Office at pg. 9, paragraph 15. Reasons follow.

In the present Office Action, the USPTO took the position that Applicants' prior amendment of claim 1 to include language from claims 10 and 12 necessitated a new ground of rejection. See the Action at pg. 9, ¶¶14-16 (setting forth the instant non-statutory double-patenting rejection). Respectfully, that position is incorrect. Applicants amended claim 1 in the face of the USPTO's stated position that claims 1-9, 15-18, 21-23, 25-26, 43-44, 55-58 and 62 were subject to the double-patenting rejection (claims 10 and 12 *were not*). See the Action dated March 11, 2004 at pg. 10, paragraph 20. Applicants relied on that position when they amended claim 1. Based on the record at the time, it should have addressed the outstanding double-patenting rejection.

However in the present Action, the USPTO took the new position that *amended* claim 1 would be rejected for non-statutory double patenting. That rejection is new because claim 1 includes language from non-rejected claims 10 and 12. Put another way, the USPTO stated in the present Action, for the first time, that claims 10 and 12 are subject to the double-patenting rejection. According to MPEP 706.07(a) a final rejection under these circumstances is not proper. Applicants are entitled to address this new basis for rejection in this case. Reconsideration and withdrawal of the finality are requested.

Claim 1 was amended with language from claims 2 and 3 (both now canceled). Remaining claims were amended, as needed, to improve claim clarity.

Claim 4 was canceled as being a substantial duplicate of claim 5.

New claims 75, 76, 77, and 78 were re-written, respectively, from claims 28, 30, 32, and 34 (now canceled).

New claims 79, 80, 81 and 82 were re-drafted, respectively, from canceled claims 36, 38, 40, and 42.

Language from claims 2 and 3 was introduced into each of new claims 75-82 in the interest of precision.

Applicants address the Examiner's concerns in the order in which they appear in the present Office Action.

#### **Prior IDS Submissions**

1. At pg. 2 of the Action, ¶4, the Office noted that an IDS submitted on January 20, 2004 (citing USP 6,593,291 to Green) was not found in the application. However, the attached return post-card clearly shows that the IDS was received by the USPTO on January 22, 2004. It should be part of the present application. Applicants respectfully request that Green be considered at this time. A duplicate copy of the IDS is being submitted herewith as a convenience.

2. Applicants also note that a subsequent IDS was submitted to the USPTO on August 19, 2004. The IDS was received prior to the mailing date of the instant action as evidenced by the attached return postcard (showing receipt on August 23, 2004). A copy of the PTO-1449 is attached to this submission as a convenience to the Examiner. Consideration of the IDS is requested.

3. Applicants further note that another IDS was submitted to the USPTO on August 23, 2004. A copy of the PTO-1449 is attached to this submission as a convenience to the Examiner. Consideration of the IDS is requested.

If the Examiner requires another copy of any reference cited above in (1)-(3), the undersigned will promptly comply once notified.

The objection to claim 13 as set forth on pg. 2, ¶5 has been addressed by this submission.

**35 USC §112, second paragraph**

Claims 1-9, 11, 13-26, 28, 30, 32, 34, 36, 38, 40 and 42-50 stand rejected as being indefinite for various reasons. Each basis of rejection is addressed in the order in which it appears on pgs. 2-4 of the action.

A. Applicants respectfully disagree with this ground of rejection. It is abundantly clear from the specification, taken as a whole, what is meant by “shown in Figure 12A (SEQ ID NOS. 73-82” and “shown in Figure 13A (SEQ ID Nos. 84-96)”.

For instance, SEQ ID No. 73, as referenced in claim 1 for example, has the following light chain sequence (taken directly from the sequence listing):

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                                <400> 73
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Gln Ser Ala Ser Leu Gly
 1               5               10               15
Glu Ser Val Thr Ile Thr Cys Trp Tyr Gln Gln Lys Pro Gly Lys Ser
 20               25               30
Pro Gln Leu Ile Tyr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
 35               40               45
Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala Glu Asp Phe
 50               55               60
Val Asn Tyr Tyr Cys Phe Gly Ala Gly Thr Lys Leu Glu Ile Lys
 65               70               75
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By inspection, one can see that SEQ ID No. 73 has the same sequence as the first line of sequence under “Light chain (LC) FR Sequences” of Figure 12A. There is certainly no ambiguity as to what sequence the claim is referring to in Figure 12A.

Similarly, SEQ ID No. 84, as referenced in claim 17, for example, has the following heavy chain sequence (taken directly from the sequence listing):

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                                <400> 84
Gln Ile Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
 1           5           10          15
Ser Val Gln Val Ser Cys Lys Thr Ser Gly Tyr Ser Phe Thr Trp Val
 20          25          30
Arg Gln Ser His Gly Lys Ser Leu Glu Trp Ile Gly Lys Ala Thr Leu
 35          40          45
Thr Val Asp Lys Ser Ser Thr Thr Ala Phe Met His Leu Asn Ser Leu
 50          55          60
Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Trp Gly Gln Gly
 65          70          75          80
                Thr Thr Val Thr Val Ser Ser
                        85
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Again by inspection, one can see that SEQ ID No. 84 has the same sequence as the first line of sequence under “Heavy chain (LC) FR Sequences” of Figure 13A. There is no ambiguity as to what sequence the claim is referring to in Figure 13A.

Correspondence between remaining lines of sequence in Figures 12A, 13A and the sequence listing of record can also be determined by inspection without any ambiguity.

Thus, a worker would understand what is meant by “shown in Figure 12A (SEQ ID NOS. 73-82)” and “shown in Figure 13A (SEQ ID Nos. 84-96)”. More specifically, that worker would know that reference was being made in the claims to a particular and ordered set of light chain and heavy chain sequences as specified in Figures 12A and

13A, respectively. No amendment to the specification or claims is needed to understand and appreciate this claim language.

**B.** The concern regarding claim 11 has been addressed by amendment.

**C.** Claim 12 has been considered indefinite for reciting “SEQ ID NO. 97”. The rejection is moot. Claim 12 has been canceled.

**D.** Claims 21-26 were deemed indefinite for reciting “at least 95% identical to” on grounds that “fractional amino acids” would be obtained. Applicants respectfully disagree.

A worker in this particular field who read the instant application would know that fractional amino acids have no meaning. Rather, the worker would consider and understand the stated identity in terms of integer values (one amino acid, two amino acids, etc.). In the event the USPTO disagrees, Applicants request that it substantiate the rejection and its position by pointing out a reference where those working in the field considered fractional amino acids as set forth in the rejection.

**E-H.** The USPTO took the position that claims 28, 30, 32, and 34 were unclear on two grounds. The first basis, relating to language in claim 17, has already been addressed above in part A. The second basis for each claim has been addressed by amendment. Specifically, each claim has been canceled in favor of new claims 75, 76, 77, and 78 respectively. Each of the new claims features antibody and light chain language from claim 17 (as amended). Heavy chain framework language (FR1-4) is from the respective canceled claims except that the Examiner’s suggestion that reference be made to SEQ ID NO. 83 has been adopted.

**I.** Claim 36 was deemed to be indefinite for not reciting “18S”. The Examiner’s suggested amendment has been adopted.

**J.** Claims 36, 38, 40, and 42 stand rejected as indefinite on two grounds. Basis for the rejection relating to claim 17 has been addressed. Each of the claims has been rewritten as new claims 79, 80, 81 and 82, respectively, using language from claim 17 (as amended). Light chain framework language (FR1-4) is from the respective canceled claim except that the Examiner's suggestion that reference be made to SEQ ID NO. 72 has been adopted.

**K.** Claim 40 stands rejected as indefinite for reciting "84A to V". The Examiner's suggested change has been incorporated into new claim 81.

**L.** Claims 45-46 have been rejected as indefinite for reciting "at least 95% identical". Applicants respectfully disagree for reasons already mentioned in part D, above.

**M.** Claim 46 stands rejected as indefinite for reasons mentioned on pg. 4 of the Action. The Examiner's suggested change has been adopted.

**N.** Claim 45 stands rejected as being indefinite for reciting "at least one complementarity determining region (CDR)". Applicants must respectfully disagree with the stated reasons for the rejection. However basis for it has been addressed by amendment.

Accordingly, reconsideration and withdrawal of each ground of rejection under §112, second paragraph, are requested.

**35 USC §112, first paragraph**

Claims 1, 6-9, 11, 13, 17-26, 28, 30, 32, 34, 36, 38, 40, and 42-50 stand rejected under §112, first paragraph, as not being enabled by the specification as filed except for a particular antibody featured at pg. 4 of the Action. Applicants must respectfully disagree with each basis of rejection.

As an initial matter, Applicants submit the rejection is moot in view of the present amendment to claims 1, 17, 45, and 46 (adding language from canceled claims 2 and 3). As formulated, claims 2 and 3 were not rejected as non-enabled. Accordingly, the rejection has been addressed in view of the record.

Applicants respectfully disagree with the rejection on further grounds.

For instance, and at pgs. 5-6 of the Action, the Office discussed the Rudikoff reference. Applicants respectfully maintain that the reference is old and out of date, particularly with respect to advances made in the field since Rudikoff published. Applicants take no position as to the merits of Rudikoff's technical findings. However, they disagree that the reference supports the enablement rejection simply because it disclosed that certain amino acid modifications may have disrupted the ligand binding of an antibody nearly 20 years ago. Nowhere in Rudikoff as relied on can Applicants find any specific teaching or suggestion that a worker could not make or use the presently claimed humanized antibodies, particularly in view of the detailed disclosure provided by the present application.

Thus to the extent the instant rejection relies on Rudikoff, it cannot stand.

At pgs. 6-7, of the Action, bridging paragraph, the Office took the position that "Applicant admits that the specification lacks guidance on how to obtain at least one murine CDR specifically because the 'best fit' methodology would not lead to elimination of up to 5 CDRs from an antibody". Applicants' respectfully disagree that such an admission has been made. Moreover, the undersigned has reviewed the prior response and can find no specific admission in this regard. Clarification is respectfully requested.

Finally, the prior response outlined how the detailed disclosure provided by Applicants satisfied the enablement requirement set forth by the CAFC (*In re Wands*) and its predecessor court the CCPA (*In re Cook and Merigold*). The present Action does not address these points. Consideration at this time is respectfully requested.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 1, 6-9, 11, 13, 17-26, 28, 30, 32, 34, 36, 38, 40, and 42-50 stand rejected under §112, first paragraph (written description). Applicants respectfully disagree.

Applicants respectfully submit the rejection is moot in view of the present amendment to claims 1, 17, 45, and 46 (adding language from canceled claims 2 and 3). Claims 2 and 3 were not rejected as not satisfying the written description requirement. Accordingly, the rejection has been addressed in view of the record.

Notwithstanding, Applicants wish to address the rejection as to the claims as currently pending.

Although Applicants are grateful that the Office took the position that Applicants are in possession of a particular antibody as set forth on pg. 7 of the Action, however, a proper application of the Guidelines entitles them to more.

For instance, and as already pointed out in the last response, Applicants stated that at least the following requirements of the Guidelines were fully satisfied by the specification as filed: **A-** Complete or Partial Structure; **B-** Other Physical and/or Chemical Properties; and **C-** Functional Characteristics Coupled with a Known or Disclosed Correlation Between Structure and Function. The instant Office Action provides no objective evidence whatsoever to suggest that a worker would not view them



in possession of the invention in view of the stated requirements.

Instead, the specification provides more than an adequate description of a variety of humanized antibodies within the scope of the pending claims. For instance, Figures 12A-D and Figures 13A-D when taken with the disclosure as a whole provide a detailed roadmap regarding many acceptable amino acid modifications that can be made to make and use the claimed humanized antibodies. In particular, detailed information on preferred FR and CDR changes are provided. This and other detailed information provided by the specification clearly evidences that Applicants were in possession of a representative number of antibody species at the time the instant application was filed.

In sum, Applicants' have fully complied with the requirements of the Guidelines especially in view of the currently amended claims.

In view thereof, reconsideration and withdrawal of the rejection are requested.

**Obviousness-type Double Patenting**

Claims 1-9, 11, 13-26, 28, 30, 32, 34, 36, 38, 40, 42, 42-58, 62, and 73-74 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 28-39 of U.S. Patent No. 6,555,319. Applicants respectfully disagree with the stated basis of the rejection. However, the rejection will be addressed once there is indication of allowable subject matter.

Examiner M. Haddad  
Group 1644  
USSN 09/990,586  
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It is believed the application is in condition for allowance, which action is earnestly solicited. Although it is not believed that any further fee is needed to consider this submission, the Office is authorized to charge such fee to our Deposit Account No. 04-1105 if deemed necessary.

Respectfully submitted,

Date: 9 Dec 2004



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Doc. 469274